May 12, 2005

Elmer Rauckman, Ph.D., DABT
Consulting Toxicologist
Ferro Corporation
1000 Lakeside Avenue
P.O. Box 147000
Cleveland, OH 44114

Dear Dr. Rauckman:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Diglyme posted on the ChemRTK HPV Challenge Program Web site on March 4, 2004. I commend Ferro Corporation for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Ferro Corporation advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission. Please send any electronic revisions or comments to the following e-mail addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If you have any questions about this response, please contact Mark Townsend, Acting Chief of the HPV Chemicals Branch, at 202-564-8617. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: M. E. Weber
J. Willis

EPA Comments on Chemical RTK HPV Challenge Submission:
Diglyme

Summary of EPA Comments

The sponsor, Ferro Corporation, submitted a test plan and robust summaries to EPA for Diglyme (CAS No. 111-96-6) dated December 31, 2003. EPA posted the submission on the ChemRTK HPV Challenge Web site on March 4, 2004.

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical Properties. The data for these endpoints are adequate for the purposes of the HPV Challenge Program.

2. Environmental Fate. The photodegradation, stability in water, and fugacity data are adequate for the purposes of the HPV Challenge Program. The biodegradation data are inadequate; however, EPA identified an adequate study that the submitter can summarize to address the endpoint.

3. Health Effects. The acute, repeated dose, and developmental toxicity data are adequate for the purposes of the HPV Challenge Program. The submitter needs to indicate the purity of the test substance so that the adequacy of the genetic and reproductive toxicity studies can be judged. In addition, the submitter needs to provide some critical information in the robust summaries.

4. Ecological Effects. EPA reserves judgement on the adequacy of all ecological endpoints pending submission of missing critical data elements in the robust summaries.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on the Diglyme Challenge Submission

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

The data for these endpoints are adequate for the purposes of the HPV Challenge Program.

Environmental Fate (photodegradation, stability in water, biodegradation, and fugacity)

The photodegradation, stability in water, and fugacity data are adequate for the purposes of the HPV Challenge Program.

Biodegradation. The data provided by the submitter are not adequate for the purposes of the HPV Challenge Program. The first study follows OECD TG 301 D "Ready Biodegradability: Closed Bottle Test". While this type of test is appropriate, the submitter only provided results for a 5-day test, not sufficient to determine ready biodegradation. The second study provided, an inherent biodegradation test, does not satisfy this endpoint because inherent biodegradation tests allow for bacterial adaptation, which does not provide a conservative picture of biodegradation of a chemical. However, EPA located a properly conducted study at the following site: http://www.cerij.or.jp/ceri_en/otoiawase/otoiawase_menu.html. The submitter needs to include a robust summary for this study in order to address the endpoint.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

The acute, repeated dose, and developmental toxicity data are adequate for the purposes of the HPV Challenge Program. The submitter needs to indicate the purity of the test substance so that the adequacy of the genetic and reproductive toxicity studies can be judged. In addition, the submitter needs to provide other critical information in the robust summaries.

Repeated-dose toxicity. EPA considers the 14-day inhalation study adequate to address this endpoint because significant concentration-related effects on male reproductive organs were seen in addition to other systemic effects in both sexes. Although the study is shorter than the SIDS-recommended duration of 28 days, a 28-day study is unlikely to provide significant new information for the Challenge program. The cited 25-day drinking water study in mice suffers from an inadequate study design.

Ecological Effects (fish, invertebrates, and algae)

EPA reserves judgement on all ecological endpoints pending submission of missing critical data elements in the robust summaries.

Specific Comments on the Robust Summaries

Health Effects

Acute Toxicity. Information missing from the robust summaries includes test substance purity, number of animals (inhalation study), and statistical methods used.

Genetic Toxicity. Information missing from the robust summaries includes test substance purity, identification of positive controls and their responses, number of replicates per concentration (gene mutations) , criteria for positive results and statistical methods used.

Ecological Effects

Fish, Daphnia, and Algae. The submitter needs to provide water quality parameters (e.g., pH, temperature, water hardness, dissolved oxygen, and alkalinity) for the duration of the studies, nominal or measured concentrations, test substance purity, and the number of organisms per exposure.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.